## REMARKS

## STATUS OF THE CLAIMS:

Claims 1 to 52, and 67 to 75 are cancelled.

Claims 53, and 56 were amended.

Claim 76 has been newly added.

Claims 53 to 66, and 76 are pending.

Clam 53 has been amended to correct a typographical error by substituting the incorrectly spelled term "complimentary" with the properly spelled term "complementary" to address the Examiners objection to the same. Claim 53 has been further amended to substitute the phrase "corresponding to" with the phrase "consisting of" in clauses "(a)", "(b)", and "(c)"; in addition to deleting clause "(d)" in its entirety to place this claim in better condition for allowance. Applicants assert that these amendments were not made to overcome any issues related to the patentability of this claim and that Applicants right to equivalents of Claim 53 is reserved. No new matter has been added.

Claim 56 has been amended to correct a typographical error by substituting the number "5" with "53" to ensure this claim properly depends from Claim 53. Applicants assert that this amendment was not made to overcome any issues related to the patentability of this claim and that Applicants right to equivalents of Claim 53 is reserved. No new matter has been added.

Support for newly added Claim 76 may be found in original Claim 53. No new matter has been added.

## I. Miscellaneous

### a. Objections to the Claims

The Examiner has objected to Applicants Claim 56 stating that "Claim 56 recites a dependency to claim 5, a claim that has been cancelled, where Applicant actually intended to describe a dependency from claim 53". Applicants agree and have amended the dependency of Claim 56 to properly depend from Claim 53. Applicants believe the Examiners objection to Claim 56 has been overcome in consideration of this amendment.

The Examiner has also objected to Claim 53 stating that "Claim 53 erroneously recites, at line 11, the term 'complimentary' where the standard usage in the relevant arts requires instead the recitation of 'complementary'". In response, Applicants have cancelled clause "(d)" within Claim 53 in its entirety. The subject matter for this clause was used as a basis for new Claim 76. Claim 76 incorporates the correct spelling of the term "complementary". Applicants believe the Examiners objection to Claim 53 has been overcome in consideration of these amendments.

### b. Public Access to ATCC Deposit No. PTA-2766

Applicants representative hereby gives the following assurance by signature below:

Bristol-Myers Squibb Company, an assignee of the present application, has deposited biological material under the terms of the Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure with the following International Depository Authority: American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209. The deposit comprises the cDNA sequence encoding the LSI-01 polypeptide of the present invention. The deposit for LSI-01 was made on December 8, 2000, and given ATCC Accession Number PTA-2766. In accordance with MPEP 2410.01 and 37 C.F.R. § 1.808, assurance is hereby given that all restrictions on the availability to the public of ATCC Accession Number PTA-2766 will be irrevocably removed upon the grant of a patent based on the captioned application, except as permitted under 37 C.F.R. § 1.808(b).

Applicants representative also hereby gives the following additional assurance by signature below:

In accordance with 37 C.F.R. § 1.805 to § 1.807, assurance is hereby given that the viability of the deposit for LSI-01, made on December 8, 2000, and given ATCC Accession Number PTA-

2766, will be maintained during the pendency of the captioned application for a duration of at least 30 years or at least five years after the most recent request for the furnishing of a sample of the deposit is received by the ATCC.

A copy of the ATCC Deposit receipt for Accession Number PTA-2766 is enclosed herewith.

## II. Rejections under 35 U.S.C. § 101

**a.** The Examiner has rejected claims 53 to 75 under 35 U.S.C. § 101, for failure to demonstrate a credible, substantial, specific, or a well-established utility. More particularly, the Examiner alleges that "the instant application cannot identify any specific, substantial, utility for the invention described by claims 53-75 known to the inventors at the time the application was filed. It is agreed that polynucleotides encoding polypeptides having the amino acid sequences described by clauses (a)-(c) of claim 53 as well as claims 54, 55 and 57-59 encode a polypeptide that shares a significant degree of amino acid sequence homology with other, prior art, mammalian serpins. Yet all of the new claims53-75 lack utility because there is no disclosure in the specification of any specific *in vitro* utility for the polypeptide product encoded by the polynucleotides of clauses (a)-(d) of claim 53, or an *in vitro* utility for their complements of clause (d) of claim 53, nor any disclosure of a specific *in vivo* utility for a polypeptide product encoded by the polynucleotides of clauses (a)-(d) of claim 53, or an *in vivo* utility for their complements of clause (d) of claim 53. While the specification proposes, at pages 4-8 and 25-32, potential uses for a claimed polynucleotide and the encoded LSI-01 polypeptide as well as various assays and processes for determining its native biological function, nowhere does the specification disclose that the native LSI-01 polypeptide has the ability to inhibit the proteolytic activity of any specific protease or any specific serine protease. While the alleged utilities are substantial, none are specific to the disclosed, native, LSI-01 polypeptide or a polynucleotide that will encode it.".

Applicants disagree. In response to the Examiners allegation that the instant specification does not identify any specific and substantial utility for the invention, Applicants wish to point to the Examiner that the instant specification does, in fact, identify a specific and substantial utility for the claimed invention. Specifically, the specification teaches that the LSI-01 "polynucleotides and polypeptides of the present invention, including agonists and/or fragments thereof, may be useful in diagnosing, treating, prognosing, and/or preventing...proliferative diseases or disorders" (see paragraph beginning on line 18, page 24). The instant specification also provides examples of such conditions by stating that "Examples of hyperproliferative diseases, disorders, and/or conditions that can be treated, prevented, and/or diagnosed by polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to neoplasms located in the...testicles..." (see paragraph beginning on line 3, page 190). The instant specification also

teaches that "Diseases associated with increased cell survival or the inhibition of apoptosis that could be treated, prevented, and/or diagnosed by the polynucleotides or polypeptides and/or antagonists or agonists of the invention, include cancers (such as...testicular cancer..." (see paragraph beginning on line 12, page 208).

Applicants assert that each of these asserted utilities are credible, substantial, and specific to the LSI-01 polynucleotides of the present invention.

Applicants assert that these utilities are "specific" since they are specific to testicular cancer, and not just any disorder. Moreover, these utilities are also specific to the claimed LSI-01 polynucleotides and polypeptides, and are not generic to members of the serpin family of proteins. Applicants also assert that these utilities are also "substantial" since testicular cancer represents a significant source of disease in humans in the world today. Applicants believe the claimed LSI-01 polynucleotides have substantial utility and does not represent a throw-away utility.

Although Applicants believe the specification, as originally filed, supports the LSI-01 polynucleotides as having a specific, substantial, and credible utility based upon the arguments presented *supra*, Applicants provide additional supporting evidence that confirms the utility of LSI-01. Applicants bring to the attention of the Examiner the Feder Declaration and its accompanying Exhibits A, and B (submitted concurrently herewith). The Feder Declaration demonstrates that LSI-01 transcripts are differentially expressed in testicular cancer tissue relative to normal testis tissue. Specifically, the Feder Declaration states that "This experiment demonstrates, unequivocally, that, LSI-01, a polynucleotide of the subject U.S. patent application, is differentially expressed in testicular cancers relative to normal testicular tissue..." (see page 1, section 3 of the Feder Declaration). The Feder Declaration also states that "LSI-01 transcripts were expressed in testicular tumors at a level that was nearly 10 times greater than the observed expression in normal testicular tissue. This data clearly confirms the utility of using LSI-01 expression as a diagnostic marker for testicular cancers." (see page 3, section 4 of the Feder Declaration). This data unequivocally confirms the utility of using LSI-01 polynucleotides as a diagnostic for testicular cancers.

Applicants point out to the Examiner that the diagnostic utility of LSI-01 polynucleotides for testicular cancers was specifically taught by Applicants specification as originally filed as discussed *supra*.

Applicants also assert that this utility was also fully enabled by Applicants specification as originally filed. Specifically, Applicants specification teaches specific methods of diagnosing diseases or disorders as demonstrated by the language of original Claim 19: "A method of

diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising: (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide." Applicants specification also teaches how one skilled in the art could measure the level of expression of the LSI-01 polypeptides in a particular sample (see Example 4).

Applicants again assert that this utility is "specific" since it is specific to testicular cancer, and not just any disorder. Moreover, these utilities are specific to the claimed LSI-01 polynucleotides, since it is the increased expression of these polynucleotides in testicular cancer tissue that substantiates their use as a diagnostic for this disorder. Applicants also assert that these utilities are also "substantial" since testicular cancer represents a significant source of disease in humans in the world today.

In addition to a specific and substantial utility, as Applicants have asserted, the Revised Utility Examination Guidelines require that such utility be credible (a "credible utility"). That is, whether the assertion of utility is believable to a person of ordinary skill in the art. Such assertions are credible unless "(A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion." See, Revised Utility Guidelines Training Materials. Applicants believe that one skilled in the art of cancer biology would credibly believe that the LSI-01 polynucleotide would have the utilities asserted by Applicants. Because Applicants have asserted specific and substantial utilities that are credible, Applicants have also complied with the credible utility requirement.

Further, PTO personnel are reminded that they must treat as true a statement of fact made by Applicants in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. Significantly, no such countervailing evidence has been provided. If such evidence is available to the examiner, Applicants request that the Examiner provide an affidavit pursuant to 37 C.F.R. § 1.104(d)(2) containing evidence substantiating this position.

Applicants further assert that this utility represents a "credible" utility as well. First, serpins are known in the art to be associated with an increased incidence of cancer and/or metastasis. The instant specification teaches that "A number of studies have shown a positive correlation between increased metastasis invasion to neighboring and systemic cells and tissues, to increased proteolytic activity of serine proteases (Testa et al., Cancer Metastasis Rev. 9:353, 1990; Dano et al., Adv.

Cancer Res. 44:139, 1985; Foekens et al., Cancer Res. 52:6101, 1992; Ossowsky, Cancer Res. 52:6754, 1992; Sumiyoshi, Int. J. Cancer 50:345, 1992; Duffy et al., Cancer Res. 50:6827, 1992; and Meissauer et al., Exp. Cell Res. 192:453, 1991). The principal serine proteases known to be associated with tumor invasion mediate the plasminogen activation cascade...The increased expression levels of uPA (urokinase plasminogen activator), the physiological substrate of alpha-anti-trypsin, has also been positively associated with increased incidence of cancers (Testa et al., Cancer Metastasis Rev. 9:353, 1990; Dano et al., Adv. Cancer Res. 44:139, 1985; Foekens et al., Cancer Res. 52:6101, 1992; Ossowsky, Cancer Res. 52:6754, 1992; Sumiyoshi, Int. J. Cancer 50:345, 1992; Duffy et al., Cancer Res. 50:6827, 1992; and Meissauer et al., Exp. Cell Res. 192:453, 1991; Heidtmann et al., Cancer Res. 49:6960, 1989; Sumiyoshi et al., Thromb Res. 63:59, 1991; Reilly et al., Int. J. Cancer 50:208, 1992, Cajot et al., Proc. Natl. Acad. Sci. USA 87:6939, 1990; Foucre et al., Br. J. Cancer 64:926, 1991; Shirasuna et al., Cancer Res. 53:147, 1993; and Janicke et al., Br. Can. Res. & Treat. 24:195, 1993)...The positive correlation between increased uPA expression on cancer incidence may have particular relevance to the LSI-01 polypeptide as the homology model of the present invention was based upon the structure of alpha-anti-trypsin, and may further suggest a use of the LSI-01 polypeptides, including fragments or antagonists thereof, in ameliorating or preventing metastasis..." (see paragraphs beginning on line 23, page 27 thru the paragraph beginning on line 20, page 28).

As the Examiner will appreciate, polynucleotides and polypeptides have a significant number of utilities above and beyond the restricted utilities cited by the Examiner. For example, a polynucleotide may be useful for diagnosing a disease or disorder in one context, while a polypeptide encoded by the same polynucleotide may be useful for treating the disorder in a different context. Significantly, Applicants are only required to provide evidence demonstrating the claimed invention has a single specific, substantial, and credible utility.

Applicants assert that the utility of LSI-01 polynucleotides as a diagnostic for testicular cancers represents a specific, substantial, and credible utility and that the Examiners rejection has been overcome in consideration of the teachings of Applicants disclosure as originally filed, the arguments presented above, in addition to the additional showing provided by the Feder Declaration.

**b.** The Examiner also alleges that "Mere allegations of a prospective, potential, utility cannot rise to the level of a credible assertion of a specific *in vivo* utility that is substantial. Indeed, the specification's diffuse assertions indicate the contrary, that Applicant knew no specific utility for either a native LSI-01 polypeptide encoded by claimed polynucleotides at the time the application was filed that would permit an immediate use by the public of a disclosed polynucleotide or any use by the public of an expression vector or host cell comprising a disclosed polynucleotide."

Applicants disagree. In response, Applicants wish to point out to the Examiner that the patent laws do not require that a specification actually demonstrate use of a claimed invention. Rather, it is established law that a disclosure is enabling so long as it contains information which would lead one of ordinary skill in the art to *reasonably believe* the claimed invention has utility. *In re Barr*, 170 U.S.P.Q. 330 (C.C.P.A. 1971). Applicants assert that one skilled in the art would reasonably believe that LSI-01 polynucleotides would have the utilities asserted by Applicants specification based upon the profound differential expression pattern of LSI-01 transcripts, the knowledge of the skilled artisan in associating mis-expression of serpins to the incidence of cancer, and the confirmation of this utility as provided by the Feder Declaration. Applicants further assert that the claimed LSI-01 polynucleotides have a specific, substantial, and credible utility based upon the arguments presented *supra.*

Similarly, there is no statutory requirement that Applicants demonstrate the physiological role of the claimed LSI-01 polynucleotides, nor a requirement that Applicants identify its native substrate. As Applicants pointed out *supra*, polynucleotides and polypeptides have a number of utilities, and Applicants are only required to provide evidence for a single, specific, substantial, and credible utility to satisfy this requirement. Applicants have provided evidence to adequately satisfy this requirement as discussed *supra.* While the identification of the physiological role of the claimed LSI-01 polynucleotides, in addition to the identification of their native substrates, would be helpful in identifying the biological pathway that is regulated by LSI-01, Applicants assert that such information could form the basis of a separate invention and is not applicable to the currently claimed invention.

As evidence to support Applicants assertion, Applicants point out that the association of a single nucleotide polymorphism to a particular disease or disorder is enough to constitute a specific, substantial, and credible utility despite that the fact that such an association requires neither the knowledge of the physiological role of the gene in which the polymorphism resides, nor the activity of the encoded protein. Despite the absence of both of the latter, such inventions clearly satisfy the

utility requirement as evidenced by the fact that claims to such associated single nucleotide polymorphisms as well as methods of using the same are routinely allowed by the USPTO with only a presentation of the statistical relevance of the association disclosed in the specification. Applicants assert that the same logical reasoning applies to the presently claimed invention and that neither the demonstration of the physiological role of the LSI-01 polynucleotide, nor the identification of its substrate, is required to meet the utility requirement. Applicants assert that the claimed LSI-01 polynucleotides have a specific, substantial, and credible utility based upon the teachings of applicants specification, the corroboration of those teachings by the Feder Declaration, and the arguments presented *supra.*

Applicants also point out that there is no requirement that Applicants preferred or best utility be disclosed in a specific location or even exemplified as representing Applicants preferred or best utility. According to the MPEP (608.01(h)), "There is no statutory requirement for the disclosure of a specific example. A patent specification is not intended nor required to be a production specification. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1536, 3 USPQ2d 1737, 1745 (Fed. Cir. 1987); *In re Gay*, 309 F.2d 768, 135 USPQ 311 (CCPA 1962). The absence of a specific working example is not necessarily evidence that the best mode has not been disclosed..." As evidenced above, Applicants have clearly disclosed a specific, substantial, and credible utility in the instant specification as originally filed, which has been corroborated by the Feder Declaration.

The Examiner further implies that Applicants specification does not support a "real world" context of use for the asserted utilities for the LSI-01 polynucleotides. Applicants do not agree and point out to the Examiner that methods of diagnosing diseases and disorders using nucleic acid- and protein-based technology is standard practice in the art of biotechnology. Moreover, Applicants also point out that testicular cancer is a real disorder afflicting a significant number of patients each year who are in need of efficacious therapies and diagnostic methods to identify and treat the same. Applicants assert that such a method constitutes a "real world" context of use and believe the Examiners allegation has been rendered moot.

Applicants believe the Examiners rejection of Claims 53 to 66 has been overcome in consideration of the arguments presented *supra.* Applicants also believe the Examiners rejection of Claims 67 to 75 has also been overcome in consideration of Applicants cancellation of the same. Applicants respectfully request that the Examiner withdraw his rejection of Claims 53 to 75 under 35 U.S.C. § 101.

## III. Rejections under 35 U.S.C. § 112, first paragraph

**a.** The Examiner has rejected Claims 53 to 75 under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner has rejected Claims 53 to 75 alleging that "since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention."

Applicants disagree and assert that the utility of LSI-01 polynucleotides as a diagnostic for testicular cancers represents a specific, substantial, and credible utility and that the Examiners rejection has been overcome in consideration of the teachings of Applicants disclosure as originally filed, the arguments presented above, in addition to the additional showing provided by the Feder Declaration.

**b.** The Examiner has rejected Claims 68 to 75 under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner states "The specification fails to exemplify or describe the preparation of variants of the LSI-01 serpin having the amino acid sequence set forth in SEQ ID NO:2 where the amino acid sequence is altered by any amino acid substitution in any of the eight amino acid sequence regions recited in claims 68-75"

Applicants disagree and point out that pages 42 to 61 of the instant specification, in conjunction with the information provided in Table IV, Figures 1A-B, Examples 5 and 21, and the level of skill of the artisan in site-directed mutagenesis methodology clearly would convince the artisan that Applicants were in possession of these variants. However, in the interest of facilitating prosecution, Applicants have cancelled Claims 68 to 75. Applicants believe the Examiners rejection of Claims 68 to 75 has been rendered moot in consideration of these amendments.

**c.** The Examiner has rejected Claims 53, and Claims 60 to 75 under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner states "Claims 53 and 60-75 rely, in part, upon deposit of a specific biological material thus presen$_t$ an issue of enablement because the specification does not disclose that the claimed biological material, the "the cDNA clone contained in ATCC Deposit No. PTA-2766" is freely available to the public, either currently or upon the issuance of a patent having the claimed biological materials as subject matter. Deposits under the terms of the Budapest Treaty are, in themselves, insufficient to satisfy 37 CFR §§1.805-1.807 unless they are disclosed on the record to be freely available to the public should a U.S. patent issue on the instant application. See, *Ex parte Hildebrand,* 15 USPQ2d 1662, 1664 (1990) (restrictions must "be irrevocably removed upon the issuance of [a] patent" since Rule 9.2 of the Budapest Treaty contains

a residual requirement of secrecy). See also, MPEP §608.01(p)(C)(3). Application of 37 CFR §1.801, et seq., to any deposit, including Budapest Treaty deposits, requires that an enabling disclosure based upon such a deposit be provided by submission of a declaration or averment, either by the assignee or the attorney of record over his or her signature and registration number, that gives these two assurances: 1) that all restrictions on the availability to the public of the deposited material will be removed, and, 2) that the viability of the deposits will be maintained, both for the duration of the patent term or for a period of twenty years in accordance with 37 CFR §§1.805-1.807."

In response, Applicants representative has provided the required assurance in the "Miscellaneous" section of Applicants Reply *supra*. The Examiner also alleges that the instant specification needs to be amended to "include specific information concerning any deposit of biological materials". Applicants do not agree and point out that the specification already provides sufficient information to adequately identify the referenced deposit, including the deposit date, accession number of the deposit, as well as the identity of the depository. Applicants assert that such information is sufficient to identify the deposit and is in accordance with MPEP 2405-2411.05 in view of *In re: Lundak, 773, F.2d, 1216, 227 USPQ 90 (Fed. Cir.* 1985).

Applicants also point out that to the Examiner that 37 CFR §1.806 requires that the deposit be maintained for a term "of at least 30 years or at least five years after the most recent request for the furnishing of a sample of the deposit is received by the depository" and is not limited to the "duration of the patent term" nor "for a period of twenty years" as alleged by the Examiner. Applicants believe the necessary assurances required for a deposit submitted in accordance with the Budapest Treaty have been met and request that the Examiner withdraw the rejection of 53, and Claims 60 to 75 under 35 U.S.C. § 112, first paragraph.

**d.** The Examiner has rejected Claims 68 to 75 under 35 U.S.C. § 112, first paragraph, alleging that these claims are "are rejected under 35 U.S.C. § 112, first paragraph, because the specification is not enabling for any embodiment of a polynucleotide that encodes a polypeptide having an amino acid sequence that diverges from the amino acid sequence of SEQ ID NO:2 as described by clauses (a)-(c) of claim 53 by amino acid substitutions in any of the eight regions recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, make and use the invention commensurate in scope with these claims."

Applicants disagree and point out that pages 42 to 61 of the instant specification, in conjunction with the information provided in Table IV, Figures 1A-B, Examples 5 and 21, and the level of skill of the artisan in site-directed mutagenesis methodology clearly would enable one skilled in the art to make and use the invention embraced by these claims. However, in the interest of

facilitating prosecution, Applicants have cancelled Claims 68 to 75. Applicants believe the Examiners rejection of Claims 68 to 75 has been rendered moot in consideration of these amendments.

## IV. Rejections under 35 U.S.C. § 112 – Second Paragraph

**a.** The Examiner has rejected Claims 53 to 75 under 35 U.S.C. § 112, second paragraph, as being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." More particularly, the Examiner alleges that Claim 53 "is indefinite in reciting "including the start codon" at the close of clause (a) because this recitation is, at best, superfluous, and at worst is ambiguous because it suggests that a polynucleotide must "includ[e] the start codon" even though the amino acid positions recited already require that a polynucleotide comprise the disclosed start codon. Claim 53 is further indefinite in reciting "minus the start codon" at the close of clause (b) because this recitation is, at best, superfluous, and at worst is ambiguous because it suggests that a polynucleotide must exclude the start codon even though the amino acid positions recited already require that a polynucleotide exclude the disclosed start codon. Claim 53 is additionally indefinite in parenthetically reciting "(antisense") because the term is ambiguous where it does not further define Applicant's intended, full-length, complementary sequences and instead suggests further, non-coding, nucleic acid sequence elements commonly used in preparing antisense constructs."

Applicants do not agree. However, in the interest of facilitating prosecution, Applicants have amended Claim 53, clause "(a)" to delete the phrase "including the start codon"; amended Claim 53, clause "(b)" to delete the phrase "minus the stop codon"; and amended Claim 53 to delete clause "(d)" in its entirety. Applicants believe the Examiners rejection of Claim 53 has been overcome in consideration of these amendments. Applicants also point out that the language of new Claim 76 explicitly Since Claims 54 to 75 depend from Claim 54 either directly or indirectly, Applicants believe the Examiners rejection of these claims has also been overcome in consideration of these amendments.

**b.** The Examiner has rejected Claim 67 under 35 U.S.C. § 112, second paragraph, as being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." More particularly, the Examiner alleges "Claim 67 is indefinite because the specification discloses at, e.g., page 2, that the polypeptide having the amino acid sequence of SEQ ID NO:2 is a serpin, an inhibitor of serine protease activity, but the claim improperly describes this polypeptide as having "serine protease" activity."

In response, Applicants have cancelled Claim 67 in the sole interest of facilitating prosecution. Applicants believe the Examiners rejection of Claim 67 has been overcome in consideration of this amendment.

**c.** The Examiner has rejected Claims 68 to 75 under 35 U.S.C. § 112, second paragraph, as being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." More particularly, the Examiner alleges "Claims 68-75 mistakenly recite subject matters that exceed the scope of claim 53 from which they depend where the preamble of claim 53 does not permit polynucleotides of clauses (a)-(d) of the claim to encode polypeptides that comprise any amino acid substitutions in the regions of SEQ ID NO:2 recited in claims 68-75. Claims 68-75 are further indefinite because claims 68, 70, 72 and 74 recite "has serpin activity", and because claims 69, 71, 73 and 75 recite "does not have serpin activity, but no claim states any particular "serpin activity" so that the artisan and the public seeking to determine the scope of these claims and the specification provides no particular disclosure that will permit a specific determination of the meaning of "serpin activity!' with which these claims might be construed."

Applicants disagree and point out that the patent laws do not require that Applicants actually demonstrate use of the present invention. However, Applicants have cancelled Claims 68 to 75 in the sole interest of facilitating prosecution. Applicants believe the Examiners rejection of Claims 68 to 75 have been overcome in consideration of these amendments.

## V. Rejections under 35 U.S.C. § 102(e)(1)

**a.** The Examiner has rejected Claim 70 under 35 U.S.C. § 102(e)(1) as being anticipated by Ni et al., U.S. 2002/0160491 and WO 2001/55390. Specifically, the Examiner alleges "The published U.S. application of Ni et al. ('091) is discussed herein rather than the identical PCT publication of Ni et al. as both are based on a U.S. provisional application filed ten months before the 14 November 2000 priority date for the instant disclosure. Ni et al. disclose a polynucleotide encoding a human serine protease inhibitor having an amino acid sequence corresponding to the 435-amino acid sequence of the LSI-01 serpin set forth in SEQ ID NO:2 herein that comprises a relative amino acid substitution at position 310, i.e., 1310V. See, SEQ IDs NOs:1 and 5 of Ni et al. Even though the polynucleotide of SEQ ID NO:I of Ni et al. encodes a serpin comprising further relative amino acid substitutions beyond the substitution at position 310 of their SEQ ID NO:2, e.g., the relative amino acid substitutions L236P, Q254H, and A348V, the disclosure of Ni et al. meets limitations of claim 70 herein for a substitution between positions 306 to 315 of SEQ ID NO:2 herein and the relationship between the subject matters of claims 68-75 and claim 53 from which they depend is ambiguous, where they embrace a scope exceeding that of claim 53, thus cannot exclude the disclosure of Ni et al."

Applicants disagree and point out that since Ni et al does not meet all of the limitations of Claim 70 ("Even though the polynucleotide of SEQ ID NO:I of Ni et al. encodes a serpin comprising further relative amino acid substitutions beyond the substitution at position 310 of their SEQ ID NO:2, e.g., the relative amino acid substitutions L236P, Q254H, and A348V"), Ni et al does not properly anticipate this claim under 35 U.S.C. § 102(e)(1). However, in the sole interest of facilitating prosecution, Applicants have cancelled Claim 70. Applicants believe the Examiners rejection of Claim 70 have been overcome in consideration of this amendment.

**b.** The Examiner has rejected Claim 70 under 35 U.S.C. § 102(e)(1) as being anticipated by Sudhiras et al., WO 2001/55390. Specifically, the Examiner alleges "Sudhiras et al. disclose a human NOV2 nucleic acid sequence encoding "a member of the serpin family", page 10, line 33, a polynucleotide encoding a human serine protease inhibitor having an amino acid sequence corresponding to the 435-amino acid sequence of the LSI-01 serpin set forth in SEQ ID NO:2 herein that comprises a relative amino acid substitution at position 310, i.e., 1310R. See, SEQ IDs NOs:3 and 4 at page 10 of Sudhiras et al. Even though the polynucleotide of SEQ ID NO:3 of Sudhiras et ai. encodes a serpin comprising further relative amino acid substitutions beyond the substitution at position 310 of their SEQ ID NO:4, e.g., the relative amino acid substitutions L236P, Q254H, and A348V, the disclosure of Sudhiras et al. meets limitations of claim 70 herein for a substitution between positions 306 to 315 of SEQ ID NO:2 herein and the relationship between the subject matters of claims 68-75 and claim 53 from which they depend is ambiguous, where they embrace a scope exceeding that of claim 53, thus cannot exclude the disclosure of Sudhiras et al."

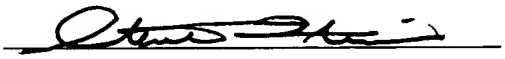
Applicants disagree and point out that since Sudhiras et al does not meet all of the limitations of Claim 70 ("Even though the polynucleotide of SEQ ID NO:3 of Sudhiras et al encodes a serpin comprising further relative amino acid substitutions beyond the substitution at position 310 of their SEQ ID NO:4, e.g., the relative amino acid substitutions L236P, Q254H, and A348V"), Sudhiras et al does not properly anticipate this claim under 35 U.S.C. § 102(e)(1). However, in the sole interest of facilitating prosecution, Applicants have cancelled Claim 70. Applicants believe the Examiners rejection of Claim 70 have been overcome in consideration of this amendment.

Applicants believe that all of the Examiners rejections and objections have been overcome and that all of the pending claims before the Examiner are in condition for allowance. An early Office Action to that effect is, therefore, earnestly solicited.

A two-month extension is hereby requested pursuant to 37 CFR §1.136(a). Please charge Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company in the amount of $430 for payment of the extension fee.

If any fee is due in connection herewith not already accounted for, please charge such fee to Deposit Account No. 19-3880 of the undersigned. Furthermore, if any extension of time not already accounted for is required, such extension is hereby petitioned for, and it is requested that any fee due for said extension be charged to the above-stated Deposit Account.

Respectfully submitted,



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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

*INTERNATIONAL FORM*

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

**To: (Name and Address of Depositor or Attorney)**

Bristol-Myers Squibb
Attn: John Feder
P.O. Box 5400
Princeton, NJ 08543

**Deposited on Behalf of:** Bristol-Myers Squibb

| **Identification Reference by Depositor:** | **Patent Deposit Designation** |
|---|---|
| Human cDNA inserts cloned into the vector pSPORT: BMS Group A | PTA-2766 |

The deposit was accompanied by: __ a scientific description _ a proposed taxonomic description indicated above.

The deposit was received December 8, 2000 by this International Depository Authority and has been accepted.

**AT YOUR REQUEST:** X We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested December 13, 2000. On that date, the culture was viable.

**International Depository Authority:** American Type Culture Collection, Manassas, VA 20110-2209 USA.

**Signature of person having authority to represent ATCC:**

**Date:** December 21, 2000

**Frank Simione, Director, Patent Depository**

**cc:** Steve Damico (Ref: Docket or Case No. D0051, D0073, D0050, D049, D0048, D0075, D0085) ✓ (7)